

Supplemental Material section

Food frequency questionnaire

Data on food intakes were obtained using a food frequency questionnaire that was administered to 536 participants with quantified PHC concentrations. The questionnaire documented their daily consumption of fish for all four seasons during the year preceding the study. For each food item, daily consumption frequency for each season and usual serving size in grams was documented. The frequency for each season was summed to obtain the average consumption frequency per day on an annual basis and the average intake in grams was calculated by multiplying the consumption frequency of the food item with the corresponding serving size. The total consumption of wild fish used in the current study corresponds to consumption of the following food items: Arctic char, cod, whitefish, trout, salmon, pike, cisco, walleye and dried fish.

Laboratory procedures for quantification of polyhalogenated compounds

The extraction and purification steps of the procedure were conducted on a Rapidtrace Automated SPE workstation (Caliper Life Science Hopkinton, MA, USA). Internal standards were added to the plasma prior to the addition of formic acid (5 ml) and deionized water (5 ml). Samples were then extracted on a Oasis HLB solid phase extraction column as described by Sandau et al. [1] and the extract was subsequently eluted through a column containing 1 g activated Florisil (Fisher Scientific, Pittsburgh, PA, USA). After drying the column with pressurized nitrogen, the sample was extracted using a methanol/dichloromethane mixture (1/9). Half of this extract was cleaned up on an activated silica/acidic silica column and the compounds were eluted with dichloromethane. The solvent was evaporated to dryness and

resulting fraction reconstituted in 5 μ L of dimethylsulfoxide for DLC analysis using the reporter gene bioassay. The second half of the SPE extract contained two fractions; 1) one with PCBs, OC pesticides and PBDEs, 2) the second containing hydroxylated and methylsulfonyl metabolites of PCBs and halogenated phenolic compounds. The fraction containing the PCBs, OC pesticides and PBDEs was eluted using hexane/dichloromethane (9/1; 9 ml). These compounds were analysed by high-resolution gas-chromatography/mass spectrometry (HRGC-MS, Agilent 6890 Network gas chromatograph (Wilmington, DE, USA) equipped with an Agilent 7683 series automatic injector and an Agilent 5973 Network mass spectrometer) using electron capture negative ionisation or electronic impact ionisation. The GC was fitted with an Agilent 60 m XLB column (0.25 mm i.d, 0.25 mm film thickness). The fraction containing hydroxylated and methylsulfonyl metabolites of PCBs and PCP was derivatised with diazomethane and cleaned up on an activated silica/acidic silica column and analysed by HRGC-MS using electron capture negative ionisation. The GC was a Hewlett Packard (HP) 5890 Series II Plus equipped with a HP G1512A automatic injector and a HP 5890B mass spectrometer (Agilent). The GC was fitted with a 30 m DB-5 column (5 % phenylmethylpolysiloxane; 0.25 mm i.d., 0.25 mm film thickness) from J&W Scientific (Folsom, CA, USA). Average recoveries were 72% for PCBs, 74% for PBDEs, 64% for organochlorine pesticides, 54% for methylsulfonyl metabolites and 53% for hydroxylated metabolites. Interassay CVs were 5%-18% for PCBs, 11%-18% for PBDEs, 2%-29% for organochlorine pesticides, 11%-38% for methylsulfonyl metabolites and 5%-31% for hydroxylated metabolites.

The limit of detection was defined as 3 times the standard deviation from ten replicates of blank matrices spiked with polyhalogenated compound levels ranging between 4 and 10 times the instrumental limit of detection, which was estimated to 3 times the signal to noise ratio.

DLC analysis

The bioassay used in our laboratory is based on the expression of the firefly luciferase in H4IIE.Luc cells resulting from the activation of the AhR pathway by dioxins. H4IIE.Luc cells (kindly donated by prof. A. Brouwer, Vrije Universiteit, Amsterdam, the Netherlands) were obtained by transfecting rat hepatoma H4IIE cells with the luciferase reporter gene plasmid pGudLuc1.1 (Aarts et al., 1995; Garrison et al., 1996). H4IIE.Luc cells were grown in 100 mm dishes in Dulbecco's Modified Eagle Medium (DMEM ; Sigma Aldrich, St-Louis, MO, USA) supplemented with 10% foetal bovine serum (Wisent Inc., St. Bruno, QC, Canada), penicillin (100 U/mL), streptomycin (100 µg/mL) and L-glutamine (292 µg/mL), in a humidified atmosphere of 5% CO₂ at 37°C. Forty-eight hours after the last dilution, the cells at 70-80% confluence were ready for use in the reporter gene assay. Cells were seeded into 24-well microplates (Sarstedt Inc., Montreal, QC, Canada) at a density of 80,000 cells per well in supplemented DMEM. After 5 hours, the medium was removed and the cells were exposed to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) (AccuStandard, New Haven, CT, USA) standards, cleaned plasma extracts or dimethyl sulfoxide (DMSO; vehicle). The final concentration of DMSO in the cell culture medium is 0.5% v/v. After the 24-hour exposure period, cells were washed with PBS 1X followed by the addition of 100 µL of lysis buffer (Passive Lysis 5× buffer; Promega, Madison, WI, USA). The plates were placed at 4°C for 30 min and then stored at -80°C overnight. On the following day, the plates containing the frozen lysates were agitated at room temperature for a few minutes, and 40 µl of the lysate was pipetted into a white 96-well microtiter plate (Dynex Technologies Ltd., Worthing, UK). The plate was then placed in a Lmax luminometer (Molecular Devices Corporation, Sunnyvale, CA, USA) and the following sequence of events was programmed for each well: a) injection of 100 µL luciferin assay mix (Promega); b) 4-sec delay; c) light production measured over a 10-sec period.

The luminescence generated by the DMSO blank was subtracted from values obtained for the 2,3,7,8-TCDD standards and the cleaned plasma extracts. TEQ concentrations for cleaned plasma extracts were interpolated from the linear portion of the standard curve (0.25-3 pM). We analysed two bovine serum samples with undetectable or very low concentrations of PCBs, PCDDs and PCDFs (#4230, Quelab, Montreal, QC, Canada) as procedural blanks and values for plasma extracts were blank corrected. The limit of detection is 30 pg TEQ/L. Although not certified for DLCs, we analysed one NIST SRM 1589a extract per batch of samples and obtained a mean concentration of 170.7 pg TEQ/L and a coefficient of variation of 26% (N = 30).

PFOS analysis

Plasma samples were spiked with PFOS-¹³C₄ (Wellington Laboratories, Guelph, ON, Canada) as the isotope-labelled internal standard for PFOS quantification. PFOS was extracted from plasma using alkaline ion-pairing extraction with methyl-tert butyl ether and tetrabutylammonium hydrogen-sulfate, followed by electrospray LC-MS-MS analysis. Separation was carried out using an Alliance 2690 high pressure liquid chromatograph (Waters Corp., Milford, MA, USA) equipped with an XTerra MS C18 column (Waters Corp.); mobile phase A was methanol and mobile phase B was a 40/60 mixture of methanol/5mM ammonium acetate. Mass spectrometry was carried out on a Micromass Quattro LC (Waters Corp.) with an electrospray source set to negative mode. The quantifier mass transition was m/z 499.0 > 99.0 and the qualifier mass transition m/z 499.0 > 169.1. As a confirmation measure, analytical specificity was determined based on the ratio between the peak area of the quantifier mass transition and the qualifier mass transition. Percent recovery for PFOS was 87%, and the limit of detection was 100 ng/L. Intraassay and interassay CVs

were 4.0% and 6.8% respectively. Interlaboratory exercises were conducted with the External Quality Assessment Scheme and the External Intercomparison Program for Toxicological Analysis in Biological Matrices (Dr. Hans Drexler).

Table S1: Linear regression models of thyroid hormones and TBG plasma levels with PCB and DLC concentrations (wet weight basis) adjusted for other families of contaminants

Weight basis) adjusted for other hormones or biomarkers									
Analytes	N	TSH		fT ₄		T ₃		TBG	
		Adjusted β (SE)		Adjusted β (SE)		Adjusted β (SE)		Adjusted β (SE)	
PCB congener									
PCB 74	621	0.044	(0.033)	-0.009	(0.007)	-0.019*	(0.008)	-0.031**	(0.010)
PCB 99	621	0.061	(0.034)	-0.002	(0.008)	-0.011	(0.008)	-0.029**	(0.011)
PCB 105	621	0.043	(0.023)	-0.007	(0.005)	-0.017**	(0.006)	-0.026**	(0.009)
PCB 118	621	0.065*	(0.033)	-0.015*	(0.007)	-0.027**	(0.009)	-0.047***	(0.012)
PCB 138	621	0.041	(0.036)	-0.005	(0.008)	-0.014	(0.008)	-0.021	(0.012)
PCB 146	621	0.014	(0.035)	-0.010	(0.007)	-0.018*	(0.008)	-0.018	(0.012)
PCB 153	621	0.015	(0.034)	-0.004	(0.008)	-0.014	(0.008)	-0.012	(0.012)
PCB 156	621	-0.014	(0.025)	-0.007	(0.006)	-0.012*	(0.006)	0.004	(0.009)
PCB 163	621	0.028	(0.034)	-0.013	(0.007)	-0.020**	(0.008)	-0.015	(0.012)
PCB 170	621	-0.008	(0.032)	-0.010	(0.007)	-0.012	(0.008)	0.012	(0.012)
PCB 172	619	0.005	(0.025)	-0.003	(0.006)	-0.011*	(0.005)	0.003	(0.009)
PCB 177	621	0.024	(0.028)	-0.007	(0.006)	-0.013*	(0.007)	-0.011	(0.009)
PCB 178	621	-0.016	(0.026)	-0.011	(0.006)	-0.017**	(0.006)	-0.001	(0.010)
PCB 180	621	-0.032	(0.031)	-0.003	(0.007)	-0.007	(0.007)	0.010	(0.011)
PCB 183	621	0.010	(0.031)	0.002	(0.008)	-0.010	(0.008)	-0.008	(0.011)
PCB 187	621	0.026	(0.036)	-0.012	(0.008)	-0.016	(0.008)	-0.014	(0.013)
PCB 194	621	-0.049	(0.026)	-0.007	(0.006)	-0.009	(0.006)	0.015	(0.010)
PCB 201	621	-0.028	(0.028)	-0.007	(0.007)	-0.013*	(0.007)	0.006	(0.011)
PCB 203	621	-0.050*	(0.025)	0.000	(0.006)	-0.005	(0.006)	0.008	(0.010)
PCB 206	621	-0.057*	(0.026)	0.001	(0.006)	0.001	(0.005)	0.024**	(0.009)
PCB grouping									
Σ PCBs	619	-0.002	(0.036)	-0.009	(0.008)	-0.018*	(0.008)	-0.007	(0.013)
Mono-ortho PCBs	623	0.048	(0.035)	-0.018*	(0.014)	-0.027**	(0.009)	-0.030*	(0.012)
DLCs	605	0.041	(0.046)	0.004	(0.010)	-0.024*	(0.011)	-0.020	(0.016)

All models adjusted for gender, age, body mass index (BMI), plasma lipids, cigarette consumption (cigarettes/day), education, PFOS and BDE-47 concentrations.

PCBs: polybrominated biphenyls, DLCs: dioxin-like compounds.

* $P \leq 0.05$, ** $P < 0.01$, *** $P < 0.001$

Table S2: Linear regression models of thyroid hormones and TBG plasma levels with HO-PCB and MeSO₂-PCB concentrations (wet weight basis) adjusted for other families of contaminants

Concentrations (wet weight basis) adjusted for other families of contaminants									
Analytes	N	TSH		fT ₄		T ₃		TBG	
		Adjusted β (SE)		Adjusted β (SE)		Adjusted β (SE)		Adjusted β (SE)	
Hydroxylated Compounds									
3-HO-PCB 138	560	0.008	(0.029)	-0.005	(0.007)	-0.023**	(0.007)	-0.015	(0.012)
3-HO-PCB 153	534	0.006	(0.032)	0.006	(0.008)	-0.019*	(0.008)	-0.019	(0.013)
4-HO-PCB 107	564	0.002	(0.034)	0.006	(0.007)	-0.009	(0.009)	-0.048***	(0.013)
4-HO-PCB 146	534	-0.008	(0.035)	-0.006	(0.008)	-0.012	(0.008)	-0.017	(0.012)
4-HO-PCB 163	565	-0.034	(0.036)	-0.005	(0.008)	-0.016	(0.009)	-0.014	(0.014)
4-HO-PCB 172	548	-0.012	(0.035)	0.001	(0.008)	-0.019*	(0.009)	-0.013	(0.013)
4-HO-PCB 187	565	-0.037	(0.035)	-0.002	(0.009)	-0.018*	(0.009)	-0.023	(0.013)
4-HO-PCB 199	566	-0.076*	(0.034)	0.002	(0.007)	-0.010	(0.008)	0.002	(0.013)
4-HO-PCB 202	564	-0.047	(0.033)	-0.002	(0.008)	-0.020*	(0.009)	-0.009	(0.015)
4-HO-PCB 208	566	-0.078*	(0.035)	0.002	(0.008)	-0.006	(0.009)	0.001	(0.013)
ΣHO-PCBs	534	-0.002	(0.040)	-0.002	(0.009)	-0.019	(0.010)	-0.029	(0.015)
Methylsulfone PCBs									
3-MeSO ₂ -PCB 49	571	0.021	(0.031)	-0.012*	(0.006)	-0.017*	(0.007)	-0.004	(0.013)
3-MeSO ₂ -PCB 87	571	0.026	(0.028)	-0.012*	(0.006)	-0.016*	(0.007)	-0.005	(0.011)
3-MeSO ₂ -PCB 101	573	0.020	(0.029)	-0.011*	(0.006)	-0.014*	(0.007)	0.005	(0.012)
ΣMeSO ₂ -PCBs	571	0.023	(0.030)	-0.012*	(0.006)	-0.017*	(0.007)	0.000	(0.012)

All models adjusted for gender, age, body mass index (BMI), plasma lipids, cigarette consumption (cigarettes/day), education, PFOS and BDE-47 concentrations.

HO-PCBs: hydroxylated metabolites of PCBs, MeSO₂-PCBs: methylsulfonyl metabolites of PCBs.

*P \leq 0.05, **P<0.01, ***P<0.001

Table S3 : Linear regression models of thyroid hormones and TBG plasma levels with organochlorine pesticides, PBDE and PFOS concentrations (wet weight basis) adjusted for other families of contaminants

PFOS concentrations (wet weight basis), adjusted for other hormones or contaminants									
Analytes	N	TSH		fT ₄		T ₃		TBG	
		Adjusted β (SE)		Adjusted β (SE)		Adjusted β (SE)		Adjusted β (SE)	
Organochlorines ^a									
<i>p,p'</i> -DDE	621	0.051	(0.037)	-0.013	(0.008)	-0.015	(0.009)	-0.023	(0.013)
Hexachlorobenzene	621	0.036	(0.034)	-0.022**	(0.007)	-0.027**	(0.009)	-0.049***	(0.011)
Pentachlorophenol	623	0.013	(0.036)	-0.002	(0.008)	-0.009	(0.011)	-0.013	(0.018)
β-HCH	620	0.081*	(0.039)	-0.013	(0.008)	-0.026**	(0.009)	-0.045***	(0.012)
PBDEs ^b									
BDE-47	621	-0.003	(0.012)	0.001	(0.003)	0.008**	(0.003)	0.003	(0.005)
BDE-153	621	-0.004	(0.022)	0.006	(0.005)	0.008	(0.005)	0.009	(0.008)
Perfluorinated compounds ^c									
PFOS	621	-0.110**	(0.042)	0.017*	(0.008)	-0.010	(0.008)	-0.029*	(0.013)

All models adjusted for gender, age, body mass index (BMI), plasma lipids, cigarette consumption (cigarettes/day) and education.

^a Further adjusted for PFOS and BDE-47 concentrations.

^b Further adjusted for PFOS and PCB-153 concentrations.

^c Further adjusted for PCB-153 and PFOS concentrations.

*P \leq 0.05, **P<0.01, ***P<0.001